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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/817,490	04/02/2004	Hsing-Pang Hsieh	70001-021001	2330

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EXAMINER	
CHONG, YONG SOO	
ART UNIT	PAPER NUMBER
1617	

NOTIFICATION DATE	DELIVERY MODE
05/21/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

INFO@ORTPATENT.COM

Office Action Summary	Application No.	Applicant(s)	
	10/817,490	HSIEH ET AL.	
	Examiner	Art Unit	
	YONG S. CHONG	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *3, 9-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-8 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

This Office Action is in response to applicant's arguments filed on 4/3/09. Claim(s) 28-32 have been cancelled. Claim(s) 1-27 are pending. Claim(s) 3, 9-26 have been withdrawn. Claim(s) 1-2, 4-8, 27 are examined herein.

Applicant's arguments have been fully considered but found not persuasive. The rejection(s) of the last Office Action are maintained for reasons of record and repeated below for Applicant's convenience.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham vs John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim(s) 1-2, 5-8 are rejected under 35 U.S.C. 103(a) as being obvious over Hwang et al. (US Patent 5,905,089) in view of Baba et al. (US Patent 6,123,943).

The instant claims are directed to a method of treating a subject with a hepatitis C virus infection by administering a composition comprising a sesquiterpene lactone of the formula in claim 5 (parthenolide).

Hwang et al. teach that parthenolide (the instantly claimed species election) inhibits Nuclear Factor - kB (NF-kB) transcription factor (example 5 on col. 14).

However, Hwang et al. fails to provide the nexus between NF-kB and hepatitis C virus infection.

Baba et al. teach the treatment of diseases upon which the NF-kB activity inhibiting action is effective (abstract). Moreover, Baba et al. that NF-kB activity inhibiting action is effective for the treatment of viral diseases (col. 3, lines 5-15), such as hepatitis (col. 8, line 30).

Examiner notes that this is a typical genus/species situation. Once a *prima facie* case of obviousness is established, the burden is shifted to the Applicant for objective evidence for nonobviousness. See MPEP 2144.08.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to have treated a person infected with hepatitis C by administering a composition comprising parthenolide.

A person of ordinary skill in the art would have been motivated to have treated a person infected with hepatitis C by administering a composition comprising parthenolide because: (1) Hwang et al. teach that parthenolide is a NF-kB inhibitor, and (2) Baba et

al. teach that NF-kB activity inhibiting action is effective for the treatment of viral diseases, such as hepatitis. Therefore, the skilled artisan would have had a reasonable expectation of success in treating a person with a hepatitis C infection by administering a composition comprising parthenolide.

Claim(s) 4 and 27 are rejected under 35 U.S.C. 103(a) as being obvious over Hwang et al. (US Patent 5,905,089) in view of Baba et al. (US Patent 6,123,943) as applied to claims 1-2, 5-8 and further in view of Tan et al. ("Hepatitis C Therapeutics: Current Status and Emerging Strategies", Nature Reviews 1:867-881, 2002, of record).

The instant claims are directed to a method of treating a subject with a hepatitis C virus infection by administering a composition comprising a sesquiterpene lactone of the formula in claim 5 and a second therapeutic agent.

Hwang and Baba et al. teach as discussed above, however, do not specifically teach a second therapeutic agent.

Tan et al. teach that IFNα-based therapies, such as Intron A, are well-known therapies for the treatment of hepatitis C virus infection (Table 1).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to have combined Intron A as taught by Tan et al. with the composition comprising parthenolide, as taught by Hwang et al. in the method of treating hepatitis C infection as taught by Baba et al.

A person of ordinary skill in the art would have been motivated to have combined Intron A as taught by Tan et al. with the composition comprising parthenolide, as taught

by Hwang et al. in the method of treating hepatitis C infection as taught by Baba et al. because of the therapeutically additive effect of using two active agents for the same purpose of treating hepatitis C infection. Therefore, the skilled artisan would have had a reasonable expectation of success in treating a subject with a hepatitis C infection by administering a composition comprising parthenolide and Intron A.

"It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... The idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Response to Arguments

Applicant argues that Hwang does not teach treating HCV infection and Baba does not teach the claimed sesuiterpene lactone compound.

In response to applicant's arguments against the references, one cannot show nonobviousness by attacking references individually where the rejections are based on the combination of references. See *In re Keller*, 642 F. 2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F. 2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant argues that Baba describes a very large number of diseases ranging from inflammatory diseases to viral disease. The reference does not specifically disclose HCV infection. Therefore, there is no motivation to select a species from a prior art genus.

This is not persuasive because the Baba reference was merely used to show that nexus between NF-kB inhibitory activity and treatment of viral disease, such as hepatitis. Thus, the rejection was not formulated to select hepatitis from a list of diseases, but was used to show that hepatitis is a disease that is related to NF-kB activity. Examiner notes on the record that the list of diseases is not very large since one of ordinary skill in the art could have readily envisioned this scenario with a reasonable expectation of success.

Applicant argues that Baba merely describes a group of 1,2,3,4-tetrahydroisoquinoline compounds that inhibit NF-kB activity. It does not show whether these NF-kB inhibitors are effective in treating any of the listed diseases, let alone HCV infection. Given the high unpredictability in the medicinal field, it is uncertain as to whether or not HCV infection could be effectively treated by inhibiting NF-kB activity. To Applicants' best knowledge, no effective anti-HCV infection drugs have yet been developed via discovering their inhibitory effects on NF-kB activity. Applicant submits Exhibit A, the Aubin reference, in corroboration that different NF-kB inhibitors may have totally different effects in treating the same disease.

A patent shall be presumed valid. Each claim of a patent (whether in independent, dependent, or multiple dependent form) shall be presumed valid independently of the validity of other claims; dependent or multiple dependent claims shall be presumed valid even though dependent upon an invalid claim. The burden of establishing invalidity of a patent or any claim thereof shall rest on the party asserting such invalidity. *35 U.S.C. 282 Presumption of Validity*

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/YONG S. CHONG/
Primary Examiner, Art Unit 1617

YSC